REMARKS

The Examiner rejected claims 33-40 and withdrew claims 1-16 from consideration. Claims 1-16 have been cancelled without prejudice, and claims 33 and 38-40 have been amended. Thus, claims 33-40 are pending. In addition, the title has been changed to coincide with the preamble of pending claims 33-40, and the original Abstract from the PCT/US98/23944 priority document has been inserted after the claims. No new matter is added by these amendments. In light of these amendments and the following remarks, Applicants respectfully request reconsideration and allowance of claims 33-40.

Election

The election of Group II (claims 33-40) made March 8, 2001 by telephone is acknowledged.

Rejections under 35 U.S.C. § 112, first paragraph

The Examiner rejected claims 33-40 under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which is most nearly connected, to make and/or use the invention. Specifically, the Examiner stated that while Applicants do provide examples in the specification of how to detect estrogen surface receptor activities such as NO and Ca^{2+} release, Applicants have not taught the artisan how to determine that the test molecule is acting specifically via an estrogen surface receptor among all the various types of endogenously expressed receptors in that cell such as opioid receptors, which also affect NO and Ca^{2+} release. The Examiner also stated that there is no guidance or working examples of how the artisan would be able to identify which specific receptor was binding, and being activated by, the test molecule, nor would it be predictable to the artisan how to determine the exact receptor being bound and activated by the ligand. In addition, the Examiner stated that Applicants have only disclosed these methods using human tissue, concluding that the claims should be limited to the use of these methods for screening agonist for human estrogen surface receptors only.

Applicants respectfully disagree. Contrary to the Examiner's assertions, Applicants' specification discloses working examples teaching how to determine the specificity of an

estrogen surface receptor response. Specifically, Example 6 starting on page 43, line 23 and extending to page 46, line 21 discloses that estrogen surface receptor responses are specifically inhibited by tamoxifen and not ICI 182,780. Thus, a person having ordinary skill in the art would have been capable of determining the presence of estrogen surface receptor-mediated responses without undue experimentation. In fact, a person having ordinary skill in the art would have been capable of following the teachings provided in Example 6 to test a molecule using the same methods used to test 17β-estradiol and E_2-BSA.

In addition, Applicants respectfully disagree with the Examiner's conclusion that the claims should be limited to screening agonists for human estrogen surface receptors because Applicants' examples used human tissue. A person having ordinary skill in the art would have been capable of following the methods described throughout Applicants' specification using tissue other than human tissue without undue experimentation. In fact, a person having ordinary skill in the art would not only have been able to replace human tissue with, for example, tissue from any common laboratory animal that produces estrogen without undue experimentation but also would have been able to test that tissue for the presence of an estrogen surface receptor using, for example, E_2-BSA and tamoxifen as taught in Example 6 of Applicants' specification without undue experimentation. Thus, Applicants' specification fully enables the presently claimed invention.

In light of the above, Applicants respectfully request withdrawal of the rejection of claims 33-40 under 35 U.S.C. § 112, first paragraph.

Rejections under 35 U.S.C. § 112, second paragraph

The Examiner rejected claims 33-40 under 35 U.S.C. § 112, second paragraph, as being incomplete for omitting essential steps. Specifically, the Examiner stated that the omitted steps are (1) the recitation of proper controls to identify that the test molecule acts specifically through estrogen surface receptors, (2) how the detection steps are to be performed, and (3) how the results are to be interpreted. In addition, the Examiner asserted that the recitation of "monitoring nitric oxide synthase activity" is vague, concluding that the claim does not recite what steps are involved in measuring this activity, nor what an increase or decrease in this activity indicates.

Applicants respectfully disagree. A person having ordinary skill in the art reading original claim 33 would have understood that no essential steps have been omitted. In fact, a person having ordinary skill in the art would have understood that the claimed methods involve contacting a cell with a test molecule and determining if that test molecule induces an estrogen surface receptor-mediated response in an estrogen surface receptor-specific manner. Moreover, a person having ordinary skill in the art would have appreciated that performing these steps can lead to the identification of an estrogen surface receptor agonist. Thus, original claim 33 recites all the essential steps required to identify an estrogen surface receptor agonist.

To further prosecution, however, claim 33 has been amended herein to recite that the induction of an estrogen surface receptor-mediated response is inhibited by tamoxifen. Claim 33 also has been amended herein to recite that the induction of an estrogen surface receptor-mediated response indicates that the test molecule is an estrogen surface receptor agonist. Thus, a person having ordinary skill in the art reading present claim 33 would have understood that present claim 33 adequately describes (1) how to determine whether or not a particular test compound induces an estrogen surface receptor-mediated response in an estrogen surface receptor-specific manner and (2) how to interpret the results in determining whether or not that particular test compound is an estrogen surface receptor agonist.

In addition, claims 38 and 40 have been amended herein to recite measuring nitric oxide release, while claims 39 and 40 have been amended to recite measuring intracellular calcium levels. Methods and materials for measuring nitric oxide release and intracellular calcium levels are disclosed throughout Applicants' specification. For example, the section starting on page 30, line 16 and extending to page 31, line 19 discloses measuring nitric oxide release, and the section starting on page 31, line 20 and extending to page 32, line 20 discloses measuring intracellular calcium levels. Thus, a person having ordinary skill in the art reading the present claims in light of Applicants' specification would have understood how the determine whether or not a particular test compound is an estrogen surface receptor agonist as presently claimed.

In light of the above, Applicants respectfully request withdrawal of the rejection of claims 33-40 under 35 U.S.C. § 112, second paragraph.

The Examiner also rejected claims 33-40 under 35 U.S.C. § 112, second paragraph, as being incomplete for omitting essential steps, stating that the claims are incomplete because cells may comprise more than one type of estrogen surface receptor and Applicants do not teach sufficient steps to determine which estrogen surface receptor the test compound is binding to and activating.

Applicants respectfully disagree. The present claims do not recite methods for determining which estrogen surface receptor the test compound is binding to and activating as the Examiner appears to contend. Instead, the present claims recite methods for identifying estrogen surface receptor agonists using cells that express an estrogen surface receptor. Again, a person having ordinary skill in the art reading the present claims in light of Applicants' specification would have understood how the determine whether or not a particular test compound is an estrogen surface receptor agonist as presently claimed.

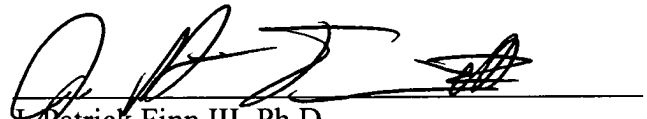
In light of the above, Applicants respectfully request withdrawal of the rejection of claims 33-40 under 35 U.S.C. § 112, second paragraph.

CONCLUSION

Applicants submit that claims 33-40 are in condition for allowance, which action is requested. Attached is a marked-up version of the changes being made by the current amendment. Please apply any charges or credits to Deposit Account No. 06-1050.

Respectfully submitted,

Date: March 8, 2002



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Version with markings to show changes made

In the specification:

The title of the specification has been changed to read as follows:

[OPIATE, CANNABINOID, AND ESTROGEN RECEPTORS] IDENTIFYING ESTROGEN SURFACE RECEPTOR AGONISTS

In the claims:

Claims 1-16 have been cancelled without prejudice.

Claims 33 and 38-40 have been amended as follows:

33. (Amended Once) A method for identifying an estrogen surface receptor agonist, said method comprising:

a) contacting a cell with a test molecule, wherein said cell expresses an estrogen surface receptor, and

b) determining if said test molecule induces an estrogen surface receptor-mediated response in said cell in an estrogen surface receptor-specific manner, wherein induction of said estrogen surface receptor-mediated response in said cell in said estrogen surface receptor-specific manner is inhibited by tamoxifen and indicates that said test molecule is said estrogen surface receptor agonist.

38. (Amended Once) The method of claim 33, wherein said determining step comprises [monitoring] measuring nitric oxide [synthase activity in] release from said cell.

39. (Amended Once) The method of claim 33, wherein said determining step comprises [monitoring] measuring intracellular calcium levels within said cell.

40. (Amended Once) The method of claim 33, wherein said determining step comprises [monitoring both] measuring nitric oxide [synthase activity] release from said cell and measuring intracellular calcium levels in said cell.